IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Shabtai Bauer	Confirmation No.: 4723
Application No.: 10/572,523	Patent No.: 7,879,800 B2
Filing Date: January 19, 2007	Patent Date: February 1, 2011
For: LARGE SCALE PREPARATION OF ALPHA-1 PROTEINASE INHIBITOR AND USE THEREOF	Attorney Docket No.: 85189-17700

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR § 1.322

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

It is requested that a Certificate of Correction be issued in connection with the above-identified patent correcting the error listed on the accompanying Form PTO-1050. The correction requested is as follows.

In Column 36, line 9 (claim 1, line 5), after "API in an aqueous medium;" start a new subparagraph with "(b) removing a portion of". Support for this change appears in application claim 1.

This request is being made pursuant to 37 CFR § 1.322 to correct an error that is clerical in nature and appears to have been made by the Office during the printing of the patent. Therefore, no fee is believed to be due for this request. Should any fees be required, however, please charge such fees to Winston & Strawn LLP Deposit Account No. 50-1814.

Respectfully submitted,

Date: February 7, 2011

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,879,800 B2

APPLICATION NO. : 10/572,523

DATED: : Feb. 1, 2011

INVENTOR(S) : Bauer

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 36:
Line 9 (claim 1, line 5), after "API in an aqueous medium;" start a new subparagraph with "(b) removing a portion of".

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The data shown in the above tables demonstrate that the decline in the percentage of the active monomeric form of API is not always reflected by the activity data obtained by the elastase assay. Therefore, API activity was evaluated by the percentage of API monomers measured by HPLC.

Graphic presentation (not shown) was used to estimate the stability of API stored in the above-described conditions after 12 and 24. The results are summarized in Table 12 below.

TABLE 12

Expected percentage of API monomers after storage for 12 month at 2-8° C.

		Percent of API Monomer		
Concentration of API, %	Concentration of Tween 80, %	Time zero	12 months	24 months
5	0	97.0	94.1	91.3
	0.01		90.2	83.1
	0.05		84.3	71.7
	0.1		77.0	57.4
10	0	96.6	90.9	85.2
	0.01		87.7	78.7
	0.05		84.6	72.6
	0.1		78.0	59.4
15	0	96.2	88.3	80.4
	0.01		84.1	72.0
	0.05		80.6	65.0
	0.1		75.4	54.6
20	0	95.6	84.2	72.8
	0.01		82.2	70.0
	0.05		78.3	61.0
	0.1		76.6	57.6

CONCLUSIONS

The use of ultrafiltration for concentrating the 2% solution obtained by the process of the present caused some generation of aggregates. Thus, the concentrated solutions already contained higher aggregate concentration at the beginning of the assay compared to the aggregate concentration in the initial 2% solution. The presence of Tween 80 in the concentrated solution caused an increase in aggregation through the storage period. This effect is concentration dependent. In addition, increase in the initial concentration of API caused an increase in the formation of aggregates. This phenomenon was observed throughout the assay, in both temperature conditions and with or without Tween 80. However, general analyses of all the data obtained clearly show that concentrated solutions of API stored at 2-8° C. are essentially stable for at least 3 months, and will maintain a good potency at this temperature for one year, even in the presence of some Tween 80. Therefore, the ready to use API-containing fluid preparation produced by the process of the present invention is highly suitable for the preparation of pharmaceutical compositions to be administered parenterally as well as by inhalation.

The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying current knowledge, readily modify and/or adapt for various applications such specific embodiments without undue experimentation and without departing from the generic concept, and, therefore, such adaptations and modifications should and are intended to be comprehended within the meaning and range of equivalents of the disclosed embodiments. It is to be understood that the phraseology or terminology employed herein is for the purpose of description and not of limitation. The means, materials, and steps for carrying out various disclosed chemical structures and functions may take a variety of alternative forms without departing from the invention.

The invention claimed is:

1. A large scale process for purifying alpha-1 proteinase inhibitor (API) from an unpurified mixture of proteins comprising:

(a) dispersing the unpurified mixture of proteins containing API in an aqueous medium (b) removing a portion of contaminating lipids and proteins by adding a lipid removal agent to the aqueous dispersion and precipitating the portion of contaminating proteins from said aqueous dispersion;

(c) loading an API-containing supernatant of step (b) containing API on a first anion exchange resin with a buffer solution having pH and conductivity such that API is retained on the first anion exchange resin;

(d) eluting an API-containing fraction from said first anion exchange resin with a same type of buffer as in step (c) having adjusted pH and conductivity;

(e) loading an API-containing fraction of step (d) on a cation exchange resin in said same type of buffer having appropriate pH and conductivity such that API is not retained on the cation exchange resin;

(f) collecting a flow-through of step (e) that contains API;

(g) loading an API-containing fraction of step (f) on a second anion exchange resin with said same type of buffer having appropriate pH and conductivity such that API binds to the second anion exchange resin; and

(h) eluting API from said second anion exchange resin with said same type of buffer having adjusted pH and conductivity to obtain a purified active API which is stable without the addition of a protein stabilizer.

2. The process of claim **1**, wherein the API comprises at least 90% active API out of the total API recovered.

3. The process of claim **2**, wherein the API comprises at least 95% active API out the total API recovered.

4. The process of claim **1**, wherein the API comprises at least 90% API out of the total protein recovered.

5. The process of claim **4**, wherein the API comprises at least 95% API out of the total protein recovered.

6. The process of claim **1**, wherein the buffer solution is other than citrate based buffer.

7. The process of claim **1**, wherein the buffer solution is acetate-based buffer.

8. The process of claim **1** further comprising a viral inactivation step.

9. The process of claim **8** wherein the viral inactivation step comprises adding a solvent and a detergent to the API of step (f) collected from the cation exchange resin.

10. The process of claim **9** wherein the detergent is a non-ionic detergent.

11. The process of claim **1**, further comprising a viral removal step.

12. The process of claim **11**, wherein the viral removing step comprises nanofiltration.

13. The process of claim **1**, wherein the unpurified mixture of proteins is selected from the group consisting of Cohn Fractions, human blood plasma and plasma fractions.

14. The process of claim **13** wherein the unpurified mixture of proteins is Cohn fraction IV-paste.

15. The process of claim **1** wherein the lipid removing agent is silicon dioxide.

16. The process of claim **1** wherein the portion of contaminating lipids and proteins is precipitated by polyalkylene glycol.